Amendments to the Specification:

Please amend the specification as follows. Insertions to the text are indicated with double underlining and deletions to the text are indicated with a strike through.

Please amend the paragraph beginning at page 7, line 3 as set forth below.

Another example of an algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul et al., J. Mol. Biol. 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information ~~(http://www.ncbi.nlm.nih.gov/)~~ website. This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul et al., supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4, and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength (W) of 3, an expectation (E) of

10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff, Proc. Natl. Acad. Sci. USA 89:10915 (1989)).

Please amend the paragraph beginning at page 8, line 25 as set forth below:

mDab1 of the present invention has been shown to comprise a phosphotyrosine binding domain and has been shown to be capable of binding to/or associating with SH2 domains of Src, Fyn and Abl. Further, the disclosed polynucleotide sequences or portions thereof can be used to identify and isolate mammalian Dab1 polynucleotide molecules from suitable hosts such as canine, ovine, bovine, caprine, lagomorph or the like. In particular, the nucleotide sequences encoding the phosphotyrosine binding domain can be used to identify poylnucleotide molecules encoding mDab1. Complementary DNA molecules encoding mDab1 may be obtained by constructing a cDNA library from mRNA ~~from~~, for example, brain. DNA molecules encoding mDab1 may be isolated from such a library using the disclosed sequences in standard hybridization techniques (e.g., Sambrook et al. ibid., and Bothwell, Yancopoulos and Alt, eds, Methods for Cloning and Analysis of Eukaryotic Genes, Jones and Bartlett Publishers, Boston, MA 1990) or by amplification of sequences using polymerase chain reaction (PCR) amplification (e.g, Loh et al. Science 243: 217-222, 1989; Frohman et al., Proc. Natl. Acad. Sci. USA 85: 8998-9002, 1988; and Erlich (ed.), PCR Technology: Principles and Applications for DNA Amplification, Stockton Press, 1989; and U.S. Patent No. 4,683,195, which are incorporated by reference herein in their entirety).

Please amend the paragraph beginning at page 9, line 11 as set forth below:

In a similar manner, genomic DNA encoding mDab1 is obtained using probes designed from the sequences disclosed herein. Suitable probes for use in identifying mDab1 sequences are obtained from mDab1-specific sequences that are highly conserved regions between murine and Drosophila Dab coding sequences. Upstream regulatory regions of mDab1 are obtained using the same methods. Suitable PCR primers are between 7-50 nucleotides in

length, more preferably between 15 and 25 nucleotides in length. Alternatively, mDab1 polynucleotide molecules may be isolated using standard hybridization ~~using~~ probes of at least about 7 nucleotides in length and up to and including the full coding sequence.

Please amend the paragraph beginning at page 15, line 20 as set forth below:

The beta amyloid precursor protein (APP) is expressed ~~is~~ as five spliced forms, all of which are transmembrane proteins. All of the splice forms have a C-terminal tail. The shortest major isoform of 165 amino acids is expressed almost exclusively in neurons and the other two major forms of 770 and 751 amino acids are expressed in both neural and non-neural cells. Abnormal cleavage of APP results in the production small peptides that lead to Alzheimer's disease (for review, see Zheng et al., Cell 81:525-531 (1995) and Selkoe, J. Biol. Chem. 271:18295-18298 (1996); which are incorporated herein by reference). The major constituent of Alzheimer's plaques is a 38-43 amino acid peptide (amyloid β-protein (Aβ)). APP is transported to the cell surface where it is either cleaved by proteolysis or endocytosed. Endocytosis of the uncleaved APP molecules is mediated by the NPXY signal sequence in the cytoplasmic tail. The endocytosis of APP is the principal path for the generation of the 38-43 amino acid peptide that is subsequently secreted and deposited in the amyloid plaques. The binding of mDab1 PTB to APP may mediate the internalization of APP by effecting the membrane flow from the surface to intracellular membrane systems, and thereby affecting the generation of Aβ. Thus, the identification of agents that mediate mDab1 binding to APP may find use in influencing the way such peptides are produced, and mutations in mDab1 may be indicative of disease.

Please amend the paragraph beginning at page 16, line 7 as set forth below:

The distribution of mDab1 ~~as~~ was determined by immunohistochemistry of hippocampal neurons, one of the cell types that are mislocalized in the mdab1 deficient mice. These neurons have a very characteristic morphology in culture with one dominant axonal trunk and several smaller dendritic off shoots. The majority of mDab1 and APP are seen in the cell

soma. APP is known to be predominantly localized in the endosomal compartment. A small fraction was also detectable at the cell surface, but this population had a short half life. APP is sorted to the axons of neurons. Interestingly mDab1 is also enriched in axons. More mDab1 immunofluorescence was observed from the midzone region of the growth cone than from dendrites. In about 5 percent of neurons mDab1 was observed in the actin rich filapodia. mDab1 and APP have a similar distribution within hippocampal neurons.

Please amend the paragraph beginning at page 19, line 12 as set forth below:

In another embodiment, the invention provides antibodies which bind to mDab1. The production of non-human antisera or monoclonal antibodies (e.g., murine, lagormorpha, porcine, equine) can be accomplished by, for example, immunizing an animal with mDab1 protein or peptides with or without an adjuvant. For the production of monoclonal antibodies, antibody producing cells are obtained from immunized animals, immortalized and screened, or screened first for the production of the antibody that binds to the mDab1 protein or peptides and then immortalized. It may be desirable to transfer the antigen binding regions (i.e., F(ab')2 or hypervariable regions) of non-human antibodies into the framework of a human antibody by recombinant DNA techniques to produce a substantially human molecule. Methods for producing such "humanized" molecules are generally well known and described in, for example, U.S. Patent No. 4,816,397; which is incorporated by reference herein in its entirety.

Please amend the paragraph beginning at page 26, line 31 as set forth below:

The three clones represented at least three different mRNAs, encoding mDab1 isoforms ~~with~~ of 555, 217 and 271 residues. The nucleotide sequences and predicted amino acid sequences of the three clones mDab555, mDab217 and mDab271 are shown in SEQ ID NO:2 and SEQ ID NO:3; SEQ ID NO:4 and SEQ ID NO:5; and SEQ ID NO:6 and SEQ ID NO:7, respectively. A comparison of the sequences shows that the mDab217 mRNA diverges from mDab555 at a consensus splice donor sequence at codon 199, encodes a further 18 residues before a termination codon, and terminates with a 3' untranslated sequence distinct from

mDab555. The mDab271 mRNA contains an additional exon of 270 nucleotides inserted between codons 241 and 242 of mDab555. This exon encodes 30 residues before a stop codon. A fragment of a potential fourth cDNA was identified using RT PCR, and contained an insert in the mDab555 mRNA at another consensus splice donor sequence between residues 239 and 242. The nucleotide sequence and deduced amino acid sequence of the exon are shown in SEQ ID NO:8 and SEQ ID NO:9.